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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/533,584

05/03/2005

Hideki Yoshikawa

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EXAMINER

NATARAJAN, MEERA

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

07/31/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/533,584	Applicant(s) YOSHIKAWA ET AL.	
	Examiner MEERA NATARAJAN	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-7 and 9-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-7, 9-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/20/2009 has been entered.
2. Claims 3-7, 9-13 are pending and will be examined on the merits.

Claim Rejections Maintained - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:
 1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Art Unit: 1643

5. Claims 1-6 and 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al. (PgPub 20040001824) in view of Zenmyo et al (Calcified Tissue Int. Vol. 67(5). pp.378-381, 2000) as evidence by Miyajii et al. (reference of record in May 5, 2005 IDS).
6. The claims are drawn to a method for inducing apoptosis in chondroma/chondrosarcoma cells, which comprises administering, to a subject in need thereof, a humanized monoclonal anti-parathyroid hormone related peptide antibody which inhibits binding of parathyroid hormone related peptide to a receptor thereof, wherein apoptosis is induced through the Bcl-2/Bax and caspase 3 pathways.
7. Yoshida et al teach a therapeutic agent for inhibiting proliferation of tumor cells stimulated by PTHrP comprising a humanized monoclonal anti-PTHrP antibody which inhibits the binding of PTHrP to its receptor (see Claims 1-20). Yoshida et al. does not teach inducing apoptosis in chondroma/chondrosarcoma cells using an anti-PTHrP antibody. This deficiency is made up for in Zenmyo et al. as evidence by Miyaji et al.
8. Zenmyo et al. teach PTHrP up-regulated the cell proliferation in chondrosarcoma cells (see Abstract and fig. 2).
9. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the antibody taught by Yoshida et al., which inhibits binding of PTHrP to its receptor, to inhibit proliferation and induce apoptosis of chondroma/chondrosarcoma cells as evidence by Miyaji et al. Miyaji et al. teach

Art Unit: 1643

administration of an anti-PTHrP humanized monoclonal antibody induces apoptosis through control of Bcl-2/Bax and caspase 3. Given the functional activity of the antibody taught by Yoshida et al., the skilled artisan would conclude that it would be inherent to the antibody claimed in Yoshida et al. to induce apoptosis through control of Bcl-2/Bax and caspase 3. Therefore, these properties are deemed inherent properties unless the applicant can prove otherwise, the burden falls on the applicant to prove that the antibodies are different because the office does not have the facilities and resources to provide the factual evidence needed to establish a difference between the claimed antibody and that disclosed by Yoshida et al. (See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd Pat. App. & Int. 1989)). One of ordinary skill in the art would have been motivated to use the antibody taught by Yoshida et al. to induce apoptosis in chondroma/chondrosarcoma cells with a reasonable expectation of success by teachings in Zenmyo et al. and Miyaji et al. because of the antitumor effects of anti-PTHrP antibodies.

Response to Arguments

10. Applicants argue that in prior art references (provided in the reply filed 05/20/2009) the anti-PTHrP1-34 antibody did not inhibit proliferation of various cell types, not including chondroma or chondrosarcoma. Applicant's argue that one skilled in the art would therefore conclude that anti-PTHrP(1-34) antibody would not affect proliferation of tumor cells. This argument has been carefully considered but not found persuasive. The references cited by Applicants are all of different tumor cell

Art Unit: 1643

types. It is evident that the anti-PTHrP1-34 antibody acts different in different cell types, as do most antibodies in regards to cancer therapy. Dackiw et al. showed that in a thyroid cancer cell line, C463, the anti-PTHrP1-34 antibody had antitumor activity although it was weak. The supporting reference, Zenmyo et al. and Miyaji et al. provide ample motivation to try the different domains of PTHrP (similar to that taught by Dackiw et al) to see if they have anti-tumor activity against chondrosarcoma cells because PTHrP up-regulated chondrosarcoma cell proliferation and an anti-PTHrP humanized monoclonal antibody induces apoptosis through control of Bcl-2/Bax and caspase 3. Therefore, the rejection of record is maintained.

Conclusion

11. Claims 3-7, 9-13 are rejected.
12. No Claim is allowed.
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is (571)270-3058. The examiner can normally be reached on Monday-Thursday, 9:30AM-7:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1643

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643